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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/589,170

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Varda Shoshan-Bar-Matz

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BUFFALO, NY 14202

EXAMINER

GREGORIO, GUINEVER S

ART UNIT

PAPER NUMBER

1732

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DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/589,170	Applicant(s) SHOSHAN-BAR-MATZ ET AL.	
	Examiner GUINEVER S. GREGORIO	Art Unit 1732	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 December 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-50 is/are pending in the application.
- 4a) Of the above claim(s) 1-39 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 40-50 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of new claims 40-50 in the reply filed on 12/01/2010 is acknowledged. The traversal is on the ground(s) that the examiner's position that the groups do not relate to a single general inventive concept citing Siebald and Gincel because the disclosed ruthenium compounds are structurally different from the instant compound and are not photoreactive. This is not found persuasive because Siebald teaches photolysis of azido compounds which corresponds with being photoreactive. Also, claim 1 does not provide a specific structure. Furthermore, as disclosed by Gincel and the art cited infra, it is well known in the art that ruthenium binds to calcium binding proteins.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-39 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected azido compound, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 11/22/2010.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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2. Claims 40-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Regarding claim 40, the phrase "optionally under photo-activation by UV radiation" renders the claim indefinite because it is unclear whether the photo-activation step is necessary for the AzRu to bind to calcium ion binding protein .

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

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under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 40-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ying et al. (Inhibition of Mitochondrial Calcium Ion transport by an Oxo-Bridged Dinuclear Ruthenium Ammine Complex; Biochemistry; 30, 4949-4952; 1991) in view of Brown et al. (Thermal and Light Induced Decomposition of Azido(bis-2,2'-bipyridine) Complexes of Ruthenium(III); Inorganic Chemistry, Vol. 14, No. 8; 1975).

8. Regarding claim 40, Ying et al. teaches ruthenium red is a well-known and effective inhibitor of the mitochondrial calcium ion uniporter (abstract). Furthermore, Ying et al. teaches a ruthenium ammine complex has a high affinity for calcium ion uniporter (page 4952, column1). Ying et al. does not teach a photoreactive azidoruthenium.

9. Regarding claims 40 and 41, Brown et al. teaches ruthenium complexes that undergo light induced reactions which corresponds with a photoreactive azidoruthenium compound (page 1915, column 1). Brown et al. teaches a mixture of and 3.09 mmol Ru(bipy)₂Cl₂ is suspended in water containing 46 mmol of sodium azide is refluxed in nitrogen for 1 hour which corresponds with a azido ruthenium compound which contains ruthenium, azido group and chlorine in the molar ration of 2:1:5 (page 1915, column 2). It would have been obvious to one of ordinary skill in the art at the time of the invention to use the photoreactive azidoruthenium taught by Brown et al. to bind to mitochondrial

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calcium ion transport taught by Ying et al. because azide radicals are highly reactive and therefore the affinity for the calcium binding protein is increased.

10. Regarding claim 42, Ying et al. teaches radiolabeled ruthenium which corresponds with an atom of said compound is a radioactive isotope (page 4950, column 2).

11. Regarding claim 43, Ying et al. teaches ^{103}Ru (abstract).

12. Regarding claims 45 and 46, Ying et al. teaches ruthenium red is a well-known and effective inhibitor of the mitochondrial calcium ion uniporter which corresponds with said compound binds to the calcium ion binding site of said calcium ion protein such as mitochondrial uniporter (abstract).

13. Claims 47-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ying et al. in view of Brown et al. as applied to claim 40 above, and further in view of Haverstick et al. (Inhibition of Human Prostate Cancer Proliferation in Vitro and in a Mouse Model by a Compound Synthesized to Block Ca^{2+} Entry; Cancer Research; 60, 1002-1008; 02/15/2000).

14. Ying et al. in view of Brown et al. teaches photoreactive azidoruthenium which can bind to calcium binding protein. Ying et al. in view of Brown et al. do not teach inhibiting treats or mitigates a disorder associated with a defect in the function of said calcium ion binding protein.

15. Regarding claims 47, 48 and 50, Haverstick et al. teaches inhibition of human prostate cancer proliferation by blocking the receptors for calcium ion (page 1002, column 1). It would have been obvious to one of ordinary skill in the art at the time of

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the invention to use the photoreactive azidoruthenium taught by Ying et al. in view of Brown et al. to block the calcium ion receptors as taught by Haverstick et al. because the blockage inhibits the proliferation of human prostate cancer.

16. Regarding claim 49, Ying et al. Brown et al. and Haverstick et al. do not teach carrier, stabilizer, adjuvant, diluent or excipient. Examiner takes the position that it is well known in the art to add various composition to stabilize molecules used for the treatment of diseases to prolong the shelf life of said molecule.

17. Claims 40-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ying et al. (Inhibition of Mitochondrial Calcium Ion transport by an Oxo-Bridged Dinuclear Ruthenium Ammine Complex; Biochemistry; 30, 4949-4952; 1991) in view of Douglas et al. (Reactions of Coordinated Ligands. II. Azide and Dinitrogen Complexes of Ruthenium; Journal of the American Society; 94:15; 1972).

18. Regarding claim 40, Ying et al. teaches ruthenium red is a well-known and effective inhibitor of the mitochondrial calcium ion uniporter (abstract). Furthermore, Ying et al. teaches a ruthenium ammine complex has a high affinity for calcium ion uniporter (page 4952, column1). Ying et al. does not teach a photoreactive azidoruthenium.

19. Regarding claims 40 and 41, Douglas et al. teaches an azido-ruthenium compound which corresponds with a azido ruthenium compound which contains ruthenium, azido group and chlorine in the molar ration of 2:1:5 (page 5254, column1 and 2). It would have been obvious to one of ordinary skill in the art at the time of the

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invention to use the photoreactive azidoruthenium taught by Douglas et al. to bind to mitochondrial calcium ion transport taught by Ying et al. because azide radicals are highly reactive and therefore the affinity for the calcium binding protein is increased.

20. Regarding claim 42, Ying et al. teaches radiolabeled ruthenium which corresponds with an atom of said compound is a radioactive isotope (page 4950, column 2).

21. Regarding claim 43, Ying et al. teaches ^{103}Ru (abstract).

22. Regarding claims 45 and 46, Ying et al. teaches ruthenium red is a well-known and effective inhibitor of the mitochondrial calcium ion uniporter which corresponds with said compound binds to the calcium ion binding site of said calcium ion protein such as mitochondrial uniporter (abstract).

23. Claims 47-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ying et al. in view of Douglas et al. as applied to claim 40 above, and further in view of Haverstick et al. (Inhibition of Human Prostate Cancer Proliferation in Vitro and in a Mouse Model by a Compound Synthesized to Block Ca^{2+} Entry; Cancer Research; 60, 1002-1008; 02/15/2000).

24. Ying et al. in view of Douglas et al. teaches photoreactive azidoruthenium which can bind to calcium binding protein. Ying et al. in view of Douglas et al. do not teach inhibiting treats or mitigates a disorder associated with a defect in the function of said calcium ion binding protein.

25. Regarding claims 47, 48 and 50, Haverstick et al. teaches inhibition of human prostate cancer proliferation by blocking the receptors for calcium ion (page 1002,

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column 1). It would have been obvious to one of ordinary skill in the art at the time of the invention to use the photoreactive azidoruthenium taught by Ying et al. in view of Brown et al. to block the calcium ion receptors as taught by Haverstick et al. because the blockage inhibits the proliferation of human prostate cancer.

26. Regarding claim 49, Ying et al. Douglas et al. and Haverstick et al. do not teach carrier, stabilizer, adjuvant, diluent or excipient. Examiner takes the position that it is well known in the art to add various composition to stabilize molecules used for the treatment of diseases to prolong the shelf life of said molecule.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GUINEVER S. GREGORIO whose telephone number is (571)270-5827. The examiner can normally be reached on Monday-Thursday, 10:30-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Curt Mayes can be reached on 571-272-1234. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gsg

January 29, 2011

/Melvin Curtis Mayes/

Supervisory Patent Examiner, Art Unit 1732